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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,479	12/08/2005	Brian Warner	BAYE0001-101	7523

28524 7590 12/11/2007

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EXAMINER	
MUMMERT, STEPHANIE KANE	

ART UNIT	PAPER NUMBER
1637	

MAIL DATE	DELIVERY MODE
12/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/525,479	WARNER ET AL.	
	Examiner	Art Unit	
	Stephanie K. Mummert, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *05 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *1-19 and 24-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/26/06;9/12/06;11/15/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of Group II, claims 20-23 in the reply filed on November 5, 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-19 and 24-31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on November 5, 2007.

Claims 20-23 are pending and will be examined.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on June 26, 2006, on September 12, 2006 and November 15, 2007 were filed in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 20-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Soderlund et al. (US Patent 6,013,431; January 2000) and further in view of Harris et al. (US Patent 5,849,544; December 1998). Soderlund teaches detection of variable nucleotides through connection to a solid support and incorporation of a labeled nucleotide (Abstract).

With regard to claim 20, Soderlund teaches a kit comprising a solid support selected from the group consisting of a solid support that comprises:

a) a capture probe and one or more target capture probes linked to the solid support at the 3' terminus directly or with spacers, one or more target capture extenders with sequences complementary to a sequence on a target capture probe and a target nucleic acid molecule, and a discrimination extender with an unblocked 3' terminus that and a sequence complementary to a sequence on a capture probe and a target nucleic acid molecule wherein the nucleotide at the 3' terminus of the discrimination extender is complementary to a single nucleotide polymorphism position of an allele;

b) a capture probe and one or more target capture probes linked to the solid support at the 5' terminus directly or with spacers (col. 4, lines 16-26, where a primer/probe is immobilized onto a solid support; col. 6, lines 28-51, where the primer is modified with an affinity moiety, preferably at the 5' end), one or more target capture extenders with sequences complementary to

a sequence on a target capture probe and a target nucleic acid molecule, and a discrimination extender with an phosphorylated 5' terminus and a sequence complementary to a sequence on a capture probe and a target nucleic acid molecule wherein the nucleotide at the 5' terminus of discrimination extender is complementary to a single nucleotide polymorphism position of an allele (col. 7, lines 14-26, where the detection step primer or discrimination extender is not modified and is complementary to the target and is complementary to the nucleotide to be detected);

c) a capture probe linked to the solid support at the 3' termini directly or with spacers, one or more target capture probes linked to the solid support at the 5' terminus directly or with spacers, one or more target capture extenders with sequences complementary to a sequence on a target capture probe and a target nucleic acid molecule, and a discrimination extender with an unblocked 3' terminus and a sequence complementary to a sequence on a capture probe and a target nucleic acid molecule wherein the nucleotide at the 3' terminus of the discrimination extender is complementary to a single nucleotide polymorphism position of an allele; and combination thereof.

With regard to claim 21, Soderlund teaches an embodiment of claim 20, wherein the solid support comprises more than one different capture probe that hybridizes to different discrimination extenders, each different capture probe spatially separated at identifiable locations and different discrimination extenders having termini complementary to a single nucleotide polymorphism position of an allele of different genes (Example 1, where more than one type of capture probe and more than one type of discrimination extender/detection primer are disclosed for the detection of more than one variable site).

With regard to claim 22, Soderlund teaches a solid support selected from the group consisting of:

a) a solid support comprising a discrimination probe linked to the solid support at the 5' termini directly or with spacers, one or more target capture probes linked to the solid support at the 5' terminus directly or with spacers (col. 4, lines 16-26, where a primer/probe is immobilized onto a solid support; col. 6, lines 28-51, where the primer is modified with an affinity moiety, preferably at the 5' end), wherein a sequence of a target probe is complementary to a sequence on a target nucleic acid molecule and a sequence on the discrimination probe is complementary to a sequence on the target nucleic acid molecule wherein the nucleotide at the 3' terminus of the discrimination probe is unblocked and complementary to a single nucleotide polymorphism position of an allele (col. 7, lines 14-26, where the detection step primer or discrimination extender is not modified and is complementary to the target and is complementary to the nucleotide to be detected);

b) a solid support comprising a discrimination probe linked to the solid support at the 3' termini directly or with spacers, one or more target capture probes and linked to the solid support at the 3' terminus directly or with spacers, wherein a sequence of a target probe is complementary to a sequence on a target nucleic acid molecule and a sequence on the discrimination probe is complementary to a sequence on the target nucleic acid molecule wherein the nucleotide at the 5' terminus of the discrimination probe is phosphorylated and complementary to a single nucleotide polymorphism position of an allele; and combinations thereof.

With regard to claim 23, Soderlund teaches an embodiment of claim 22, wherein the solid support comprises more than one different discrimination probe, each different discrimination

probe spatially separated at identifiable locations and different discrimination extenders having termini complementary to a single nucleotide polymorphism position of an allele of different genes (Example 1, where more than one type of capture probe and more than one type of discrimination extender/detection primer are disclosed for the detection of more than one variable site).

Regarding claims 20-23, Soderlund does not specifically teach the element wherein the capture probes have terminal nucleotides that are blocked and/or unphosphorylated. Harris teaches the use of capture probes where the 3' end is blocked through immobilization while the 5' end is rendered incapable of ligation or extension via lack of a phosphoryl group or through blockage with a variety of 5' substituents (col. 5, line 46 to col. 6, line 5). Harris also teaches the reverse set up, where the capture probe is immobilized at the 5' end and blocked at the 3' end with suitable substituents to prevent reaction at the 3' end.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the capture probes so that they were blocked or unphosphorylated to prevent extension of these primers during the extension or discrimination phase of the solid phase assay. As taught by Harris, "the capture probe is incapable of participation in the amplification stage. For example, it may be a capture oligodeoxynucleotide in which the 3' end is chemically bonded to the wall of the reaction vessel or bonded to solid phase material" (col. 5, lines 50-62). Therefore, it would have been obvious to employ methods known in the art to prevent primer extension or other reaction, including blocking terminal nucleotides or dephosphorylating nucleotides at the 5' end.

2. Claims 20-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Urdea et al. (US Patent 5,635,352; June 1997) in view of Soderlund et al. (US Patent 6,013,431; January 2000) and Harris et al. (US Patent 5,849,544; December 1998). Urdea teaches a method for nucleic acid detection and signal amplification to reduce background (Abstract).

With regard to claim 20, Urdea teaches a kit comprising a solid support selected from the group consisting of a solid support that comprises:

a) a capture probe and one or more target capture probes linked to the solid support at the 3' terminus directly or with spacers, one or more target capture extenders with sequences complementary to a sequence on a target capture probe and a target nucleic acid molecule, and a discrimination extender with an unblocked 3' terminus that and a sequence complementary to a sequence on a capture probe and a target nucleic acid molecule (Figure 10, and col. 13, line 44 to col. 15, line 49, where capture probes are linked to the solid support, capture extender probes are complementary to a target and on the capture probe);

b) a capture probe and one or more target capture probes linked to the solid support at the 5' terminus directly or with spacers, one or more target capture extenders with sequences complementary to a sequence on a target capture probe and a target nucleic acid molecule, and a discrimination extender with an phosphorylated 5' terminus and a sequence complementary to a sequence on a capture probe and a target nucleic acid molecule;

c) a capture probe linked to the solid support at the 3' termini directly or with spacers, one or more target capture probes linked to the solid support at the 5' terminus directly or with spacers, one or more target capture extenders with sequences complementary to a sequence on a target capture probe and a target nucleic acid molecule, and a discrimination extender with an

unblocked 3' terminus and a sequence complementary to a sequence on a capture probe and a target nucleic acid molecule (Figure 10, and col. 13, line 44 to col. 15, line 49, where capture probes are linked to the solid support, capture extender probes are complementary to a target and on the capture probe).

With regard to claim 22, Urdea teaches a solid support selected from the group consisting of: a) a solid support comprising a discrimination probe linked to the solid support at the 5' termini directly or with spacers, one or more target capture probes linked to the solid support at the 5' terminus directly or with spacers, wherein a sequence of a target probe is complementary to a sequence on a target nucleic acid molecule and a sequence on the discrimination probe is complementary to a sequence on the target nucleic acid molecule (Figure 10, and col. 13, line 44 to col. 15, line 49, where capture probes are linked to the solid support, capture extender probes are complementary to a target and on the capture probe);

b) a solid support comprising a discrimination probe linked to the solid support at the 3' termini directly or with spacers, one or more target capture probes and linked to the solid support at the 3' terminus directly or with spacers, wherein a sequence of a target probe is complementary to a sequence on a target nucleic acid molecule and a sequence on the discrimination probe is complementary to a sequence on the target nucleic acid molecule (Figure 10, and col. 13, line 44 to col. 15, line 49, where capture probes are linked to the solid support, capture extender probes are complementary to a target and on the capture probe).

Regarding claims 20-23, Urdea does not teach that the discrimination probe is complementary to a single nucleotide polymorphism. Soderlund teaches a discrimination extender probe wherein the nucleotide at the 3' terminus of the discrimination extender is

complementary to a single nucleotide polymorphism position of an allele (col. 7, lines 14-26, where the detection step primer or discrimination extender is not modified and is complementary to the target and is complementary to the nucleotide to be detected).

With regard to claim 21 and 23, Soderlund teaches an embodiment of claim 20 or 22, wherein the solid support comprises more than one different discrimination probe, each different discrimination probe spatially separated at identifiable locations and different discrimination extenders having termini complementary to a single nucleotide polymorphism position of an allele of different genes (Example 1, where more than one type of capture probe and more than one type of discrimination extender/detection primer are disclosed for the detection of more than one variable site).

Regarding claims 20-23, neither Urdea or Soderlund specifically teach the element wherein the capture probes have terminal nucleotides that are blocked and/or unphosphorylated. Harris teaches the use of capture probes where the 3' end is blocked through immobilization while the 5' end is rendered incapable of ligation or extension via lack of a phosphoryl group or through blockage with a variety of 5' substituents (col. 5, line 46 to col. 6, line 5). Harris also teaches the reverse set up, where the capture probe is immobilized at the 5' end and blocked at the 3' end with suitable substituents to prevent reaction at the 3' end.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have applied the technique of detection of variable nucleotides as taught by Soderlund into the method of Urdea to arrive at the claimed invention with a reasonable expectation for success. Both Urdea and Soderlund are focused on the inclusion of a solid support for the detection of nucleic acids. As taught by Urdea, "the invention is useful in

conjunction with any number of assay formats wherein multiple hybridization steps are carried out to produce a detectable signal which correlates with the presence or quantity of a polynucleotide analyte" (col. 1, lines 39-43), while Soderlund teaches "the detection step primers are preferably selected so as to span the region immediately toward the 3' end from the variable nucleotide to be detected" (Abstract). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have applied the technique of detection of variable nucleotides as taught by Soderlund into the method of Urdea to arrive at the claimed invention with a reasonable expectation for success.

Furthermore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the capture probes so that they were blocked or unphosphorylated to prevent extension of these primers during the extension or discrimination phase of the solid phase assay. As taught by Harris, "the capture probe is incapable of participation in the amplification stage. For example, it may be a capture oligodeoxynucleotide in which the 3' end is chemically bonded to the wall of the reaction vessel or bonded to solid phase material" (col. 5, lines 50-62). Therefore, it would have been obvious to employ methods known in the art to prevent primer extension or other reaction, including blocking terminal nucleotides or dephosphorylating nucleotides at the 5' end.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephanie K. Mummert, Ph.D. whose telephone number is 571-272-8503. The examiner can normally be reached on M-F, 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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